

## PATENT SPECIFICATION

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## COMPLETE SPECIFICATION

## Parasiticidal Lotions.

We, MCKESSON & ROBBINS, INCORPORATED, a Corporation duly organized under the laws of the State of Maryland, United States of America, of Bridgeport, Connecticut, United States of America (Assignees of ALLEN L. OMOHUNDRO and FRANZ M. NEUMEIER, both citizens of the United States of America and respectively of Wilton, Fairfield County, Connecticut, 5 10 United States of America, and Fairfield, Fairfield County, Connecticut, United States of America) do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement :—

The present invention relates to a process for producing a parasiticidal lotion for combating such body parasites as head and 20 body lice. Heretofore insecticidal preparations have been proposed in which kerosene extract of pyrethrum has been mixed with rotenone, cyclohexanone, higher secondary alcohols  $C_{10}-C_{16}$ , oil of sesame, 25 shell oil P81, chondrus extract, water Tee-pol, hydroquinone and kerosene. It has also previously been proposed to provide an improved form of concentrate containing such a high concentration of pyrethrins 30 that it will be effective as an insecticide for use as a spray against mosquitoes at high dilution. One such proposed concentrate has been composed of pyrethrum extract  $\beta$ -dichloro-diphenyl-trichlorethane, sesame 35 oil, methyl nonyl ketone, geraniol, heavy naphtha, Lissolamine, hydroquinone and pyrocatechol. These proposed compositions do not contain an intermiscible solvent within the meaning of our invention. 40 The object of the present invention is to provide a preparation containing pyrethrum extract, which is effective as a parasiticide and 2, 4-dinitroanisole acting as an ovicide. 45 Other objects of the invention are to provide a lotion which is quickly effective as [Price]

a parasiticide, which is clear, homogeneous and stable, which manifests no adverse skin reaction, which is easy to apply and easy to remove, which is free from grease 50 and which in general lends itself satisfactorily to the strictest pharmaceutical requirements.

In accordance with the invention a process of producing a parasiticidal lotion for 55 body parasites consists in mixing together pyrethrum extract, sesamin extract, an ovicide, a solvent for said ovicide, water as a dispersion medium for said extracts, an intermiscible solvent and agents for emulsifying the mixture to produce a clear, 60 stable, homogenous lotion.

According to a further feature of the invention the process consists in mixing together pyrethrum extract, a sesamin extract, 65 apiol, dinitroanisole, benzyl alcohol, an intermiscible solvent, water and agents for emulsifying the mixture to produce a clear, stable homogenous lotion.

In the lotion according to the invention 70 the pyrethrum extract serves as an active parasiticidal ingredient, the sesamin extract has a synergistic or activating action on the pyrethrins of the pyrethrum extract, the apiol has an insecticidal effect, the dinitroanisole serves as an ovicide, and the benzyl alcohol which serves as a solvent for the dinitroanisole affords an anaesthetic effect. 75

The mixture which preferably also contains perfume oils may be clear or cloudy depending for the most part on the wax content of the pyrethrum extract and on the solvent used in the manufacture of this extract. The dewaxed purified pyrethrum 80 extract as used for aerosol bombs yields mostly clear mixtures.

In order to make the mixture described above emulsifiable, an intermiscible solvent has to be used. The solvent may be either 85 oleic acid or a glycol monolaurate or propylene glycol monooleate. Lotions, accord-

ing to the invention, prepared by using one or more of the above-mentioned emulsifiers may on occasion be non-transparent, depending on the fat and wax content of 5 the naturally occurring pyrethrum extract. In order to maintain the correct hydrophilic-lipophilic ratio necessary to produce transparency, it is necessary to add a small amount of a material acting as an inter- 10 miscible solvent. An intermiscible solvent is a material by means of which more than one non-miscible substance can be coupled to yield a clear and homogeneous solution. The material acting as an intermiscible 15 solvent can by modification of the hydrophilic-lipophilic ratio effect transparency.

The process according to the invention starts with two different phases, namely, the phase of pyrethrum extract with or 20 without apiole and the phase consisting of benzyl alcohol, sesamin extract and dinitroanisole. The intermiscible solvent (oleic acid) couples these two phases and is necessary to maintain clarity and homogeneity. 25 The resulting solution must be emulsified. The emulsifying agents for that purpose must be slightly acid and acid-stable to produce a lotion having a final pH of approximately 5.5—6.5 which is the range 30 of optimum stability of pyrethrins. The emulsifying agents are desirably a combination of at least two of the following classes:

1. Sulfonated or sulfated oils such as 35 castor oil, corn oil, cottonseed oil, etc.
2. Derivatives of hexahydric alcohol anhydride partial esters, namely sorbitan or mannnitan monolaurate, such derivatives being condensation products with ethylene oxide. The sum of such ethylene oxide linkages add up to 20 mols per mol of sorbitan or mannnitan monolaurate.
3. Dioctyl sulfosuccinate and desirably the sodium salt, such as that described in 45 the U.S. Patent No. 2,028,091.

For example, sulfonated oil may be combined with dioctyl sodium sulfosuccinate; sulfonated oil with the derivatives of hexahydric alcohol anhydride partial esters; or 50 the latter compound with dioctyl sodium sulfosuccinate to produce the necessary emulsification.

The different ingredients of the lotion are dispersed in a diluent such as water. 55 The resulting mixture aside from the emulsifying agents and the intermiscible solvent is not clear or stable, since it comprises a number of immiscible liquids. Therefore, to bring all of the ingredients of the mixture with water together in the form of a 60 clear and stable emulsion, it has been found advantageous to employ two emulsifying agents and it is necessary to employ an intermiscible solvent as described above.

65 The pyrethrum extract containing pyre-

thrins may be of any suitable type, and is desirably a dewaxed product containing about 20% pyrethrins. If the pyrethrum extract used yields a cloudy lotion, this can be corrected to produce a clear product by 70 the use of additional organic solvents in a concentration of not more than 2% by weight at the expense of the water content of the formula. These solvents should be of such a nature as to prevent the waxes 75 and polymerization products, as found in the commercially available pyrethrum extract, from precipitating out of the lotion. These solvents may be, for example, acetone, cyclohexanone, carbon tetrachloride, 80 chloroform, alkylated naphthalenes and others.

The sesamin extract may contain in total from 11 to 25% of sesamin solids. The sesamin solids desirably contain an average 85 of 90% of pure sesamin.

The apiole (dimethyl methylene ether of allyl tetroxybenzene) which is employed is desirably oleoresin of parsley fruit (liquid apiole). Apiole in this form has the advantage of not crystallizing out of the lotion. However, as far as certain aspects of the invention are concerned, crystalline apiole may be employed, although for lotion purposes, it is not as desirable as liquid apiole. 95

The apiole can be dissolved in the pyrethrum extract since the latter contains kerosene as a dissolving medium, in which apiole is also soluble.

Dinitroanisole is employed as a ovicide 100 to destroy the nits or eggs of the parasites. Benzyl alcohol is used as a solvent for the dinitroanisole. This alcohol also has a slight anaesthetic effect which is desirable. Benzyl alcohol is also desirable for use as 105 a solvent for the dinitroanisole, because a suspension of pure sesamin crystals in sesame oil was found soluble in benzyl alcohol.

The odor of the lotion may be improved 110 by using a mixture of essential oils.

The following examples are illustrations of formulations in accordance with the present invention, but they are not to be construed as limiting the invention:— 115

EXAMPLE 1.	
Using Sulfonated Oil and Dioctyl Sodium Sulfosuccinate as Emulsifying Agents	% weight/weight
Pyrethrum Extract, dewaxed (20% pyrethrins)	120 5.0
Apiole (Oleoresin Parsley)	0.5
Sesamin Extract	0.25
Propylene glycol monolaurate	8.0
Dioctyl-Sodium-sulfosuccinate	3.0 125
Sulfonated corn oil, sulfonated castor oil or sulfonated cotton seed oil	20.0
2, 4-Dinitroanisole	1.0
Benzyl Alcohol	130

(Free from Chlorine) 8.0  
 Perfume Oils 1.0  
 Distilled water q.s. 100% (appr. 53.0)

## EXAMPLE 2.

5 Using Sulfonated Oil and Derivatives of Hexahydric Alcohol Anhydride Partial Esters

	% weight/weight
10	Pyrethrum Extract (as above) 5.0
	Apiole (Oleoresin Parsley) 0.5
	Sesamin Extract 0.25
	Propylene Glycol Monolaurate 5.0
15	Sorbitan or Mannitan Mono-laurate Polyoxyalkylene Derivatives 20.0
	Sulfonated Corn Oil or sulfonated Castor Oil 10.0
	2, 4-Dinitroanisole 1.0
20	Benzyl Alcohol 8.0
	Perfume Oils 1.0
	Distilled Water q.s. 100% (appr. 47.0)

## EXAMPLE 3.

Same as example 2 except that propylene glycol monolaurate is replaced by 4% oleic acid and the water adjusted accordingly.

## EXAMPLE 4.

Using Derivatives of Hexahydric Alcohol Anhydride Partial Esters and Dioctyl Sodium Sulfosuccinate

	% weight/weight
30	Pyrethrum Extract 5.0
	Apiole 0.5
	Sesamin Extract 0.25
	Propylene Glycol Monolaurate 6.0
35	Dioctyl-Sodium-Sulfosuccinate 18.0
	Sorbitan or Mannitan Mono-laurate Polyoxyalkylene Derivatives 10.0
	2, 4Dinitroanisole 1.0
40	Benzyl Alcohol 8.0
	Perfume Oils 1.0
	Distilled Water q.s. 100% (appr. 50.0)

## EXAMPLE 5.

Same as example 4 except that the propylene glycol monolaurate is replaced by oleic acid 3.5% and the water is adjusted accordingly.

A procedure which may be employed for making a batch of the lotion in accordance with the formulation above set forth, is as follows:

1. Mix together dinitroanisole, sesamin extract and benzyl alcohol. If the resulting mixture is not clear after standing for 55 a while, filter to get a clear solution.

2. Mix together the pyrethrum extract, apiole and the intermiscible solvent (either oleic acid or propylene glycol monolaurate) and add to solution from step 1. Add perfume oils and mix. In cases where the pyrethrum extract is of such a nature as to render the final lotion cloudy, add the additional solvent for the extract such as acetone, cyclohexanone or the like, as referred 65 to above.

3. Add the two emulsifying agents and mix.
4. Add water and mix until a clear solution is obtained.

A pyrethrum lotion as described is 70 thoroughly efficient and quickly effective in combating body and head lice, even in the most severe cases, is stabilized against decomposition, and remains clear and homogeneous indefinitely at temperatures above 75 15°C. When this lotion is applied, the lice die quickly. These applications are attended without dermatitis or skin irritation. The parasiticidal action of the lotion is decisive, and nits contacted with this lotion are 80 killed and fail to incubate.

In the application of the lotion, one or two ounces of this lotion, applied, as for example, to the infected head of a person, is allowed to remain for about ten to fifteen 85 minutes. At the end of that period, the medication may be removed with water, or if desired, soap and water may be used. It was found by this medication process, that the lice were killed, and that the nits did 90 not incubate at the end of the hatching period.

Since the lotion of the present invention is clear and homogeneous, it is not necessary to shake it before use. In the case of a 95 suspension which has to be shaken before use, there is no assurance that the active ingredients will be applied to the affected part in the right proportions. Furthermore, with a suspension, there are solid 100 particles which are not easy to wash off. The lotion of the present invention, on the other hand, contains detergents which serve to produce foam so that the lotion works like a shampoo. A great deal of foam is 105 produced in its application, and this carries all foreign matter out of the hair. In other words, the emulsifying agents serve not only to afford a clear lotion, but also permit said lotion with all the foreign matter 110 attached thereto to be washed off. This is important where hair is being treated.

What we claim is:—

1. A process of producing a parasiticidal lotion for body parasites consisting in 115 mixing together pyrethrum extract, sesamin extract, an ovicide, a solvent for said ovicide, water as a dispersion medium for said extracts, an intermiscible solvent and agents for emulsifying the mixture to produce a clear, stable and homogenous lotion.

2. A process of producing a parasiticidal lotion for body parasites consisting in mixing together pyrethrum extract, sesamin extract, apiole, dinitroanisole, benzyl alcohol, 125 an intermiscible solvent, water and agents for emulsifying the mixture to produce a clear, stable, homogenous lotion.

3. A process of producing a parasiticidal lotion for body parasites consisting in mix-

- ing together pyrethrum extract, an additional organic solvent for said extract of the type which will prevent the waxes, polymerization products and other ingredients of the extract from precipitating out of the lotion, and which aids in rendering the final product clear, sesamin extract, an ovicide, a solvent for said ovicide, an intermiscible solvent for said ingredients, water 10 as a dispersion medium and agents for emulsifying the mixture to produce a clear, stable, homogenous lotion.
4. A process according to Claim 1 wherein at least one of said emulsifying agents 15 is a sulfonated vegetable oil.
5. A process according to Claim 1 wherein at least one of said emulsifying agents is a derivative of hexahydric alcohol anhydride partial esters and is a condensation 20 product with ethylene oxide.
6. A process according to Claim 1 wherein at least one of said emulsifying agents is dioctyl sulfosuccinate.
7. A process according to Claim 1 where- 25 in said intermiscible solvent is oleic acid.
8. A process according to Claim 1 wherein said intermiscible solvent is a glycol fatty ester.
9. A parasiticidal lotion for body para- 30 sites when made according to the process claimed in any of Claims 1 to 8.
10. A process according to Claim 2 wherein said emulsifying agents include a sulfonated vegetable oil and a derivative of 35 hexahydric alcohol anhydride partial esters, said derivative being a condensation product with ethylene oxide.
11. A process according to Claim 2 wherein said emulsifying agents include a sul- 40 fonated vegetable oil and dioctyl sulfosuc- cinate.
12. A process according to Claim 2 wherein said emulsifying agents include a derivative of hexahydric alcohol anhydride 45 partial esters and dioctyl sulfosuccinate, said derivative being a condensation product with ethylene oxide.
13. A process according to Claim 2 wherein said intermiscible solvent is oleic 50 acid and said emulsifying agents include a sulfonated vegetable oil and a derivative of hexahydric alcohol anhydride partial esters, said derivative being a condensation product with ethylene oxide.
14. A process according to Claim 2 55 wherein said intermiscible solvent is oleic acid and said emulsifying agents include a sulfonated vegetable oil and dioctyl sulfosuccinate.
15. A process according to Claim 2 60 wherein said intermiscible solvent is oleic acid and said emulsifying agents include a derivative of hexahydric alcohol anhydride partial esters and dioctyl sulfosuccinate, said derivative being a condensation product with ethylene oxide.
16. A process according to Claim 2 65 wherein said intermiscible solvent is a glycol fatty acid ester and said emulsifying agents include a sulfonated vegetable oil and a derivative of hexahydric alcohol anhydride partial esters, said derivative being a condensation product with ethylene oxide.
17. A process according to Claim 2 70 wherein said intermiscible solvent is a glycol fatty ester and said emulsifying agents include a sulfonated vegetable oil and dioctyl sulfosuccinate.
18. A process according to Claim 2 75 wherein said intermiscible solvent is a glycol fatty acid ester and said emulsifying agents include a derivative of hexahydric alcohol anhydride partial esters and dioctyl sulfosuccinate, said derivative being a condensation product with ethylene oxide.
19. A parasiticidal lotion for body para- 80 sites when made according to the process claimed in any of Claims 10 to 18.
20. A parasiticidal lotion for body para- 85 sites when made according to the process claimed in Claim 3.
21. A process of producing a parasiticidal lotion for body parasites substantially as hereinbefore described with reference to examples 1, 2, 3, 4 or 5.

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